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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/425,742	10/22/1999	KARL THEODOR KRAEMER	DEAV1998/L071 US NP	9957

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EXAMINER	
YU, GINA C	

ART UNIT	PAPER NUMBER
1617	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/425,742	KRAEMER ET AL.	
	Examiner	Art Unit	
	GINA C. YU	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23,28,29 and 39-44* is/are pending in the application.

4a) Of the above claim(s) *3,9 and 41-44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-8,10-23,28,29,39 and 40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 11, 2008 has been entered.

Election/Restrictions

According to Office action dated November 15, 2000, paper no. 7, applicant has elected in response to species election requirement the following film-forming agent and plasticizer: 1) vinylimidazolium methochloride/vinylpyrrolidone copolymer; and 2) polyethoxylated hydrogenated castor oil.

Claims 1, 7, 8, 11-21 are considered generic to the species set forth, and claims 3, 9, 10, 39, 43, and 44 are withdrawn from consideration as these are directed to non-elected species.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1, 2, 4-8, 11-14, 22, 23, 28, 29, and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gaillard-Kelly (US 4946870) ("Gaillard") in view

of Partain (US 4946870), Smith (US 5658559) ,and Cremophor RH 40 Technical Information (1997).

Gaillard teaches that the phenylimidazolidines of instant formula I have anti-androgenic activity and are used in pharmaceutical compositions including creams, pomades, and lotions. See col. 9, lines 29 – 36. Example 96 teaches 4-[3-(4-hydroxybutyl)-2,5-dioxo-1-imidazolidinyl]-2-(trifluoromethyl)benzonitrile. See instant claim 4. The reference teaches that the compositions useful for treatment of acne and androgenic alopecia, among others. See col. 9, lines 43 – 55. The reference specifically teaches that the compositions are "useful in dermatology" and can be used with other anti-acne components such as retinol or with a product stimulating the growth of hair such as Minoxidil (6-amino-4-4-piperidino-1, 2-dihydro-1-hydroxy-2-iminopyridimidine) for the treatment of alopecia. See col. 9, lines 56 – 65. See instant claims 11, 13, and 23.

Partain teaches a topical film-forming composition for delivering pharmaceutical actives with controlled release. The reference teaches that the composition is useful as a delivery system for single or combination of pharmaceutical active agents, including anti-acne agents (retinoic acid and benzoyl peroxide) and anti-alopecia agents (Minoxidil). See col. 9, lines 15 –16; Examples 1, 15, and 18. See instant claims 22, 23, 28, and 29. Partain also teaches using the delivery system for either single or combination of pharmaceutical agents. Particularly mentioned pharmaceutical actives are diazoxide, nifedipine and diltiazem; angiotensins (captopril). See col. 8, lines 55 – 58; col. 9, line 2; instant claims 11-14.The reference teaches that chitosan derivatives

are useful film formers and topically applied in the form of lotion, solution, cream, etc. See col. 3, lines 28 – 52. The polymer is said to readily form a film and "acts as a reservoir to continuously deliver the actives as well as protect the tissue from further injury or insult", which negates the need of hair cover. The reference goes on to teach that the film gives uniform distribution of the active on the tissue and prevents the migration or loss of the active from the site of application, and helps to control the dosage at a constant level. The reference also teaches using solvents such as ethanol or and glycerin with the chitosan film-forming agent. See col. 9, line 58 –66; col. 10, lines 10-17; Example 14; instant claim 8.

Although Partain provides the general teaching of using a film-forming agent to formulate a controlled-release delivery system for anti-acne agents and anti-alopecia agents, either alone or in combination with other pharmaceutical agents, the reference does not mention the specific type of the film-forming polymer which the present applicant has elected for the prosecution.

Smith also teaches a film-forming lotion composition which forms barrier on the surface of the skin to prevent evaporative loss of moisture from the skin, and protects the skin from environmental irritants. The reference teaches polyquaternary polyvinylpyrrolidone such as polyquaternium-16 (polyvinylpyrrolidone/imidazolinium methochloride copolymers). See instant claim 40. Isopropanol is used as a solvent to dissolve pharmaceutical actives. See examples I and II; instant claim 8. The therapeutic agents include anti-acne actives including benzoyl peroxide and vitamin A. See col. 5, lines 1-6.

The references fail to teach the specific type of the elected plasticizer, polyoxyethylated hydrogenated castor oil.

Cremophor RH 40 Technical Information (Cremophor) teaches that POE hydrogenated castor oil is skin compatible and solubilizes hydrophobic pharmaceuticals including vitamin A (retinoic acid). See Solubilization. The reference teaches that the product forms clear solutions in water and ethanol with fatty acids and fatty alcohols. See Solubility. Gaillard further teaches adding to the composition 5 alpha-reductase inhibitor, which meets instant claims 16 and 17. See col. 9, lines 56 – 61.

Partain and Smith would have obviously motivated one of ordinary skill in the art at the time the present invention to modify the teaching of Gaillard and formulate the active ingredients in a controlled-release composition because (a) Partain teaches that a film-forming composition "acts as a reservoir to continuously and uniformly deliver the actives as well as protect the tissue from further injury or insult, which negates the need of hair cover, and controls the dosage at a constant level; (b) Smith also teaches a film-forming formulation which provides controlled-release of the actives while protecting the skin and prevent loss of moisture of the skin. The skilled artisan would have had a reasonable expectation of successfully producing a stable and effective film-forming lotion which is useful for treating acne or alopecia, and delivering the active agents in a controlled, constant dosage, while protecting the application site.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the composition of the combined references by adding to the composition POE hydrogenated castor oil as motivated by Cremophor because (a)

Smith, Gaillard, and Cremophor all teach using retinoic acid; and (b) Cremophor teaches that POE hydrogenated castor oil is a well known solubilizer in pharmaceutical/cosmetic art, which solubilizes hydrophobic pharmaceutical agents to form a clear solution. The skilled artisan would have had a reasonable expectation of successfully producing a stable, clear cosmetic composition comprising retinoic acid and the compound of instant formula (I).

Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gaillard, Partain, Smith and Cremophor as applied to claims 1, 2, 4-8, 11-14, 22, 23, 28, 29, and 40 as above, and further in view of Ismail (US 5541220).

The combined references fail to teach methylxanthine compounds.

Ismail teach agents for the treatment protection of the skin. Exemplified is a capsule that can treat alopecia, which comprises pentoxifylin, vitamin E, and other ingredients.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the composition of the combined references by adding pentoxifylin to the composition of the combined references as motivated by Ismail because a) Gaillard and Ismail are directed to treating alopecia; and b) Ismail teach pentoxifyiline as increasing blood circulation which is used in an alopecia treatment composition. The skilled artisan would have had a reasonable expectation of successfully producing an alopecia treatment composition which increases blood circulation and aids circulating the active agents of the composition though the body.

Claims 18 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gaillard, Partain, Smith and Cremophor as applied to claims 1, 2, 4-8, 11-14, 22, 23, 28, 29, and 40 as above, and further in view of Gaetani et al. (EP 0427625 A).

Gaillard teaches to combine phenylimidazolidines with a product stimulating the growth of hair for the treatment of alopecia. See col. 9, lines 55 – 65. The reference fails to teach 2,4-diamino-6-butoxy-3-sulfopyrimidine hydroxide.

Gaetani teaches internal salts of 2,4-diamino-6-alkoxy-3-sulfoxypyridimine hydroxide for combating hair loss and inducing/stimulating hair growth. See abstract. Specifically disclosed is 2,4-diamino-6-butoxy-3-sulfoxypyridimidine hydroxide. See Example de composition 2 and 3.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the composition of the combined references by adding 2,4-diamino-6-butoxy-3-sulfopyrimidine hydroxide to the composition, as motivated by Gaetani because (a) both Gaillard and Gaetani are directed toward combating hair loss; and (b) Gaillard teaches to combine phenylimidazolidines with hair growth stimulating agents to make an anti-alopecia composition. The skilled artisan would have had a reasonable expectation of successfully producing an improved anti-alopecia composition which combats hair loss and promotes hair growth.

Claims 18 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gaillard, Partain, Smith and Cremophor as applied to claims 1, 2, 4-8, 11-14,

22, 23, 28, 29, and 40 as above, and further in view of applicants' own disclosure and Hocquaux et al. (WO 92/21317).

Gaillard teaches to combine phenylimidazolidines with a product which stimulates the growth of hair for the treatment of alopecia. See col. 9, lines 55 – 65. The combined references fail to teach 2, 6-diamono-4-piperidinopyridine.

Hocquaux ('317) teaches compositions containing a pyridine-1-oxide compound for combating hair loss and inducing/stimulating hair growth. See '701, abstract. 2,6-diamino 4-peperdinopyridine 1-oxide is disclosed in Example 1. See instant claims 18 and 20.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the composition of the combined references by adding 2,6-diamino 4-peperdinopyridine 1-oxide to the composition because (a) both Gaillard and Hocquaux are directed toward combating hair loss; and (b) Gaillard teaches to combine phenylimidazolidines with other hair growth stimulating agents to make an anti-alopecia composition. The skilled artisan would have had a reasonable expectation of successfully producing an improved anti-alopecia composition which combats hair loss and promotes hair growth.

Claims 18 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gaillard, Partain, Smith and Cremophor as applied to claims 1, 2, 4-8, 11-14, 22, 23, 28, 29, and 40 as above, and further in view of Hocquaux et al. (WO 91/19701).

Gaillard teaches to combine phenylimidazolidines with a product stimulating the growth of hair for the treatment of alopecia. See col. 9, lines 55 – 65. The combined references fail to teach 2,6-diamino-4-butoxy-1,3,5-triazine 1-oxide.

Hocquaux ('701) teaches compositions containing 2, 6-diamino-1,3,5-triazine derivatives for combating hair loss and inducing/stimulating hair growth. See abstract. 2,6-diamino-4-butoxy-1,3,5-triazine 1-oxide is disclosed in Examples.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the composition of the combined references by adding 2,6-diamino-4-butoxy-1,3,5-triazine 1-oxide to the composition because (a) both Gaillard and Hocquaux are directed toward combating hair loss; and (b) Gaillard teaches to combine phenylimidazolidines with other hair growth stimulating agents to make an anti-alopecia composition. The skilled artisan would have had a reasonable expectation of successfully producing an improved anti-alopecia composition which combats hair loss and promotes hair growth.

Response to Arguments

Applicant's arguments filed on September 26, 2006 have been fully considered but they are moot in view of the new grounds of rejection in part and not persuasive in part.

Partain in view of Gaillard

Applicant asserts that the Office bears the burden of showing glycerin in Partain functions as a plasticizer. Examiner respectfully disagrees, as glycerin is an art-

recognized plasticizer used in controlled-release composition which softens the film which the composition forms. See US 5451673 A. However, the rejection is withdrawn in order to comply with the species election requirement made in November 15, 2000, paper no. 7, and the arguments are moot.

Gaillard-Kelly in view of Smith

Applicant's argument that glycerin is not a plasticizer is moot as the rejection is withdrawn.

Claim 14

Applicant asserts that Lai fails to teach combining captopril with anti-alopecia agents. Applicant's argument is moot in view of a new ground of rejection as discussed above.

Claim 15

Applicant asserts that Ismail fails to cure the alleged deficiency of the Partain/Gaillard rejection, which is now withdrawn. The argument is moot in view of the new ground of rejection.

Claims 18 and 19

Applicant asserts that Gaetani fails to cure the alleged deficiency of the Partain/Gaillard rejection, which is now withdrawn. The argument is moot in view of the new ground of rejection.

Claims 18 and 20

Applicant asserts that Hocquaux ('317) fails to cure the alleged deficiency of the Partain/Gaillard rejection, which is now withdrawn. The argument is moot in view of the new ground of rejection.

Claims 18 and 21

Applicant asserts that Hocquaux ('701) fails to cure the alleged deficiency of the Partain/Gaillard rejection, which is now withdrawn. The argument is moot in view of the new ground of rejection.

Claims 5 and 6

Applicant asserts that Cremophor fails to cure the alleged deficiency of the Partain/Gaillard rejection, which is now withdrawn. The argument is moot in view of the new ground of rejection.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to GINA C. YU whose telephone number is (571)272-8605. The examiner can normally be reached on Monday through Friday, from 8:00AM until 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Gina C. Yu/
Primary Examiner, Art Unit 1617